The L1 adhesion molecule normalizes neuritogenesis in Rett syndrome-derived neural precursor cells.

Journal: Biochem Biophys Res Commun

Publication Year: 2017

Authors: Myungsik Yoo, Cassiano Carromeu, Ohyoon Kwon, Alysson Muotri, Melitta Schachner

PubMed link: 29050935

Funding Grants: Developing a drug-screening system for Autism Spectrum Disorders using human neurons, A drug-screening platform for autism spectrum disorders using human astrocytes

Public Summary:
In this work we showed that ectopic expression of the L1 cell adhesion molecule could rescue some of the cellular phenotypes in Rett syndrome. This unusual link might be explored as a novel therapeutic opportunity.

Scientific Abstract:
Therapeutic intervention is an important need in ameliorating the severe consequences of Rett Syndrome (RTT), a neurological disorder caused by mutations in the X-linked gene methyl-CpG-binding protein-2 (MeCP2). Following previously observed morphological defects in induced pluripotent stem cell (iPSC)-derived neurons obtained from female RTT patients, we hypothesized transfection with the L1 cell adhesion molecule (L1) could contribute to normalizing a pathological male cell system bearing a nonsense mutation of MeCP2. We found a decreased expression of L1 in RTT iPSCs-derived neural precursor cells (RTT NPCs) and decreased neuritogenesis. Expression of wild-type MeCP2 in RTT NPCs revealed a positive correlation between the levels of MeCP2 and L1 and normalization of cell survival. Expression of L1 in RTT NPCs enhanced neuritogenesis and soma size. Knock-down of MeCP2 in wild type NPCs reduced neuritogenesis. L1 expression is regulated by the MeCP2 promoter. These results suggest that a deficiency in L1 may partially account for RTT phenotypes.